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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/716,824	11/19/2003	Paul O. Sheppard	97-11D1	8035

7590 07/10/2006

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EXAMINER	
REDDIG, PETER J	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 07/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/716,824	SHEPPARD ET AL.	
	Examiner	Art Unit	
	Peter J. Reddig	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) *1-4 and 12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-11* is/are rejected.

7)☒ Claim(s) *8* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/20/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The response filed on May 2, 2006 to the restriction requirement of April 24, 2006 has been entered. Applicant has elected Group III, claims 5-11 drawn to an antibody that specifically binds ONE Zsig9 polypeptide and method to produce said antibody, the polypeptide being SEQ ID NO: 2, for examination. Because applicant did not distinctly and specifically point out any supposed errors in the restriction requirement, the election has been treated as an election without traverse MPEP 818.03(a).

Claims 1-12 are pending.

Claims 1-4 and 12 are hereby withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to a non-elected invention.

Claims 5-11 are currently under consideration.

Specification Objections

2. The disclosure is objected to because of the following informalities:

The specification on page 1 should be amended to reflect the status of the parent application serial number 09/489,101. It should state:

The present application is a divisional of U.S. Patent Application Serial No. 10/082,502, filed October 19, 2001, now abandoned, which is a continuation of U.S. Patent10 Application Serial No. 09/318,028 filed May 25 1999, now abandoned, which is a continuation-in-part of U.S. Patent Application Serial No. 09/109,808 filed July 2, 1998, now abandoned, which claims the benefit of U.S. Provisional Application No. 60/089,899, filed June 17, 1998, U.S. Provisional

15 Application No. 60/085,983 filed May 19, 1998 and U.S. Provisional Application No. 60/051,704 filed July 3, 1997.

The word "acid" is omitted on p. 2 line 19.

Appropriate correction is required.

Claim Objections

3. Claim 8 is objected to because of the following informalities: The word "or" on line 8 of Claim 8 appears to be misspelled and should be "of". Appropriate correction is required.

Claim Rejections - 35 USC § 101

4. 35 U.S.C. §101 states:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 5, 6, and 9 are rejected under 35 USC §101 because the claimed invention is directed to a non-statutory subject matter. The antibody as claimed has the same characteristics as antibodies found naturally.

The claims, as written, do not sufficiently distinguish over antibodies that exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hands of man, an antibody against the polypeptide defined by the amino acid sequence of SEQ ID NO: 2 is considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by

insertion of the term "isolated" or "purified," provided no new matter is introduced. See MPEP 2105.

5. Claims 5-11 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by any of a substantial utility, a well-established utility or a specific asserted utility.

The disclosed utilities for SEQ ID NO: 2 are enhancing the growth or development of the placenta, heart, and liver (p.27, 5th para.), cancer diagnosis and therapy (pp.33-35) and to reduce restenosis (p35, 2nd para). However, neither the specification nor any art of record teaches what the SEQ ID NO: 2 is, what it does do, do not teach a relationship to any specific diseases or establish any involvement in the etiology of any specific diseases. Further, the asserted utilities for SEQ ID NO: 2, such as screening of agonists and antagonists (p.27, 4th para.) and production of antibodies (p. 44, para. 2) apply to many unrelated polypeptide structures sequences. Therefore these asserted utilities are not considered specific utilities, i.e. they are not specific to SEQ ID NO: 2.

As drawn to the usefulness of the SEQ ID NO: 2 polypeptide for enhancing the growth or development of the placenta, heart, and liver, no specific working examples are presented drawn to the ability of SEQ ID NO: 2 to enhance the growth and development of these tissues. Furthermore, the specification does not teach about the relation of the structure of SEQ ID NO: 2 to the growth or development of these tissues. No evidence has been presented drawn to a nexus between SEQ ID NO: 2 and enhancing the growth or development of the placenta, heart, and

liver, thus additional work must be done in order to determine if in fact SEQ ID NO: 2 is associated with these things and thus the SEQ ID NO: 2 does not have substantial utility.

The specification also speculates that if the Zsig9 polypeptide or anti-Zsig9 antibody targets vascular cells or tissues, such polypeptide or antibody may be conjugated with a radionuclide, and particularly with a beta-emitting radionuclide, to reduce restenosis.

As drawn to the reduction of restenosis in vascular tissue, no data or working examples are presented drawn to the expression of the SEQ ID NO: 2 polypeptide in vascular tissue. Furthermore, the specification does not teach about the structure or function of the SEQ ID NO: 2 polypeptide in relation to the etiology of restenosis. Only teachings of general treatments for restenosis are given, p. 35 para. 2. Thus no evidence has been presented drawn to a nexus between SEQ ID NO: 2 and reduction of restenosis, thus additional work must be done in order to determine if in fact SEQ ID NO: 2 is associated with these things and thus the SEQ ID NO: 2 does not have substantial utility.

The asserted utility of SEQ ID NO: 2 appears to be based on (1) the identity of SEQ ID NO: 2 to amylin and CGRP, both members of a hormone peptide family with similarity of structure and some overlap of function and (p. 39, 1st para) (2) the overexpression of mRNA encoding SEQ ID NO: 2 in tumor cells compared to normal control suggesting that SEQ ID NO: 2 is useful as a tumor diagnostic, therapeutic (p.40, 2nd para.).

(1) The asserted utility of the SEQ ID NO: 2 polypeptide is based on the assertion that SEQ ID NO: 2 has structural identity to the hormones/growth factors amylin and CGRP. However, a review of the following databases (A_Geneseq_21, Issued_Patents_AA, Published_Applications_AA_Main, Published_Applications_AA_New,

Pending_Patents_AA_Main, Pending_Patents_AA_New, PIR_80, UniProt_05.80) has not revealed any identity of SEQ ID NO: 2 to either Amylin or CGRP even though the search revealed identities as low as 13.4%. Although the specification hypothesizes that the claimed protein might be involved in homeostasis and may be activated to alleviate stress, apparently because of a putative identity to amylin or CGRP, neither the specification nor the art of record teach what SEQ ID NO: 2 is or does and does teach any relationship to a specific disease or to an etiology of any specific disease. It is clear that given this clear lack of identity wherein it does not appear that the claimed SEQ ID NO: 2 has an identity even as great as 13.4 % to amylin or CGRP. It is also clear that the claimed protein has at least a lack of similarity or identity of 86.6 % and the effects of this dissimilarity upon protein structure and function cannot be predicted.

Bowie et al (Science, 1990, 257:1306-1310) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function and carry out the instructions of the genome and further teaches that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. (col 1, p. 1306). Bowie et al further teach that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (col 2, p. 1306). The sensitivity of proteins to alterations of even a single amino acid in a sequence are exemplified by Burgess et al (J of Cell

Bio. 111:2129-2138, 1990) who teach that replacement of a single lysine reside at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein and by Lazar et al (Molecular and Cellular Biology, 1988, 8:1247-1252) who teach that in transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen. These references demonstrate that even a single amino acid substitution will often dramatically affect the biological activity and characteristics of a protein. Clearly, with at least 86.6 % dissimilarity, to amylin and CGRP, the function of the SEQ ID NO: 2 polypeptide could not be predicted, based on sequence similarity with Amylin/CGRP, nor would it be expected to be the same as that of amylin and CGRP. Further, Scott et al (Nature Genetics, 1999, 21:440-443) teach that the gene causing Pendred syndrome encodes a putative transmembrane protein designated pendrin. Based on sequence similarity data, the authors postulated that the putative protein was deemed to be a member of sulfate transport protein family since the putative protein had a 29% identity to rat sulfate-anion transporter, 32% similarity to human diastrophic dysplasia sulfate transporter and 45% similarity to the human sulfate transporter. However, upon analyzing the expression and kinetics of the protein, the data revealed no evidence of sulfate transport activity wherein results revealed that pendrin functioned as a transporter of chloride and iodide. Scott et al suggest that these results underscore the importance of confirming the function of newly identified gene products even when database searched reveal significant homology to proteins of known function (page 411, 1st column, 4th paragraph). In addition, Bork (Genome Research, 2000,10:398-400) clearly teaches the pitfalls associated with

comparative sequence analysis for predicting protein function because of the known error margins for high-throughput computational methods. Bork specifically teaches that computational sequence analysis is far from perfect, despite the fact that sequencing itself is highly automated and accurate (p. 398, col 1). One of the reasons for the inaccuracy is that the quality of data in public sequence databases is still insufficient. This is particularly true for data on protein function. Protein function is context dependent, and both molecular and cellular aspects have to be considered (p. 398, col 2). Conclusions from the comparison analysis are often stretched with regard to protein products (p. 398, col 3). Furthermore, recent studies show that alternative splicing might affect more than 30% of human genes and the number of known post-translational modifications of gene products is increasing constantly so that complexity at protein level is enormous. Each of these modifications may change the function of respective gene products drastically (p. 399, col 1). Further, although gene annotation via sequence database searches is already a routine job, even here the error rate is considerable (p. 399, col 2). Most features predicted with an accuracy of greater than 70% are of structural nature and at best only indirectly imply a certain functionality (see legend for table 1, page 399). As more sequences are added and as errors accumulate and propagate it becomes more difficult to infer correct function from the many possibilities revealed by database search (p. 399para bridging cols 2 and 3). The reference finally cautions that although the current methods seem to capture important features and explain general trends, 30% of those features are missing or predicted wrongly. This has to be kept in mind when processing the results further (p. 400, para bridging cols 1 and 2). The teachings of Bork are clearly illustrated by US Pub **20030105000** which specifically teaches on page 73 that the SH2 domain of Grb14 is 81% similar to the SH2 domain

of Grb7 on the amino acid level, but although Grb7 binds to ErbB2, Grb14 does bind to ErbB2. Further, although the SH2 domain of Grb2 is only 50 % similarity to Brb 7 on the amino acid level, both Grb2 and Grb7 bind to the same site on ErbB2. Thus, sequence identity or similarity alone cannot be used to predict the function of a protein.

Clearly, given not only the teachings of Bowie et al, Lazar et al, Burgess et al, Scott et al. and US Publication 2003010500 but also the limitations and pitfalls of using computational sequence analysis and the unknown effects of alternative splicing, post translational modification and cellular context on protein function as taught by Bork, clearly with a 86.6 % dissimilarity to amylin and CGRP, the function of the SEQ ID NO: 2 polypeptide could not be predicted, based on sequence similarity with amylin and CGRP, nor would it be expected to be the same as that of amylin and CGRP. Further, even if the polypeptide of SEQ ID NO: 2 is found to be an amylin-like or CGRP like protein, neither the specification nor any art of record teaches what the polypeptide is, what it does, does not teach a relationship to any specific disease or establish any involvement of the polypeptide in the etiology of any specific disease. Given the above, it is clear that additional work must be done in order to establish that SEQ ID NO: 2 functions in any manner similar to the members of the amylin and CGRP family and thus the claimed invention does not have substantial utility. Further, given the limited identity to the members of the amylin and CGRP family, it is clear, for the reasons set forth above, that SEQ ID NO: 2 does not have a well-established utility based on its identity to said family.

(2). As drawn to the asserted utilities of SEQ ID NO: 2, based on the overexpression of mRNA encoding SEQ ID NO: 2 in tumor cells compared to normal control, the specification teaches that the overexpression of the SEQ ID NO: 2 at the mRNA level indicates that this

polypeptide and its corresponding antibodies can be useful for the detection and/or treatment OF cancer using the methods described in the specification (p.33-35). However, the art recognizes that the regulation of mRNA translation is one of the major regulatory steps in the control of gene expression, Jansen, et al. (Pediatric Res., 1995, 37 (6): 681-686). Further, those of skill in the art, recognize that expression of mRNA, specific for a tissue type, does not dictate not predict the translation of such mRNA into a polypeptide. For example, Alberts et al. (Molecular Biology of the Cell, 3rd edition, 1994, p. 465) teach that translation of ferritin mRNA into ferritin polypeptide is blocked during periods of iron starvation. Likewise, if excess iron is available, the transferring receptor mRNA is degraded and no transferrin receptor polypeptide is translated. Many other proteins are regulated at the translational level rather than the transcriptional level. For instance, Shantz and Pegg (Int. J. of Biochem. and Cell Biol., 1999, 31: 107-122) teach that ornithine decarboxylase is highly regulated in the cell at the level of translation and that translation of ornithine decarboxylase mRNA is dependent on the secondary structure of the mRNA and the availability of e IF-4E, which mediates translation initiation. McClean and Hill (Eur. J. of Cancer, 1993, 29A: 2243-2248) teach that p-glycoprotein can be overexpressed in CHO cells following exposure to radiation, without any concomitant overexpression of the p-glycoprtein mRNA. In addition, Fu et al. (EMBO J., 1996, 15:43982-4401) teach that levels of p53 protein expression do not correlate with levels of p53 mRNA levels in blast cells taken from patients with acute myelogenous leukemia, said patients being without mutation in the p53 gene. As drawn specifically to cancer, Brennan et al. (J. Autoimmunity, 1989, 2 (suppl.): 177-186) teach that high levels of the mRNA for TNF alpha were produced in synovial cells, but that levels of the TNF alpha protein were undetectable. Thus, protein translation is not necessarily

contingent on mRNA expression due to the multitude of homeostatic factors affecting transcription and translation. Given the above, it is not clear from the teaching of the specification that the protein to which the claimed antibody binds is even expressed in vivo and thus the claimed invention does not have substantial utility because additional work must be done to determine if the protein is expressed in vivo.

Further, even if the protein is expressed in vivo, the art recognizes that protein levels do not correlate with steady state mRNA levels or alterations in mRNA levels in both cancer and normal cell types. For instance, once again, Brennan et al. (J. Autoimmunity, 1989, 2 (suppl.): 177-186) teach that high levels of the mRNA for TNF alpha were produced in synovial cells, but that the TNF alpha protein was undetectable. Zimmer (Cell Motility and the Cytoskeleton, 1991. 20:325-337) teaches that there is no correlation between the mRNA level of calcium-modulated protein S1000 alpha and the protein level, indicating that S100 protein is post-transcriptionally regulated. Eriksson et al. (Diabetologia, 1992, 35: 143-47) teach that no correlation was observed between the level of mRNA transcript from the insulin-responsive glucose transporter gene and the protein encoded thereby. Hell et al. (Laboratory Investigation, 1995, &3: 492-496) teach that cells in all types of Hodgkin's disease exhibited high levels of bcl-2 mRNA, while the expression of the Bcl-2 protein was not homogenous to said cells. Powell et al. (Pharmacogenesis, 1999, 8:411-421) teach that mRNA levels for cytochrome p450 E1 did not correlate with the level of corresponding protein, and conclude that the regulation of said protein is highly complex. Carrere et al. (Gut, 1999, 44: 550-551) teach an absence of correlation between protein and mRNA levels of the Reg protein. Vallejo et al. (Biochimie, 2000 82:1129-1133) teach that no correlation was found between NRF-2 mRNA and protein levels suggesting

post-transcriptional regulation of NRF-2 protein levels. Guo et al. (J. Pharmacol. Exp. Ther. 2002, 300: 206-212) teach that Oat p2 mRNA levels did not show a correlation with Oatp2 protein levels, suggesting that the regulation of the OATp2 protein occurs at both the transcriptional and post-translational level. These references serve to demonstrate that levels of RNAs cannot be relied upon to anticipate levels of protein. Further, Jang et al. (Clinical Exp. Metastasis, 1997, 15: 469-483) teach that further studies are necessary to determine if changes in protein levels track with changes in mRNA levels for metastasis associated gene in murine tumor cells, thus providing further evidence that one of skill in the art cannot anticipate that the level of a specific mRNA expressed by a cell will be paralleled at the protein level. Thus it is clear that additional work must be done in order to establish that SEQ ID NO:2 is differentially expressed in cancer cells compared to normal controls so that it could be successfully used as a target for diagnosis and or treatment of cancer.

Thus it is clear that additional work must be done in order to establish what SEQ ID NO: 2 is, what it does and/or to establish a relationship of SEQ ID NO: 2 to any specific diseases or to establish its involvement in the etiology of any specific diseases, thus SEQ ID NO: 2 does not have a substantial utility. Further, since it is unknown what SEQ ID NO: 2 is, what it does, what its relationship is to any specific diseases or the etiology of any specific diseases, it is clear that SEQ ID NO: 2 does not have a well established utility. The specification essentially gives an invitation to experiment wherein the artisan is invited to elaborate a functional use for the disclosed SEQ ID NO: 2. Because SEQ ID NO: 2 is not supported by a specific asserted utility for the reasons set forth, credibility of any utility cannot be assessed. Further, given that SEQ ID NO: 2 has none of substantial, specific, and well-established utility, credibility of any utility

cannot be assessed, it is clear that antibody to SEQ ID NO: 2 also has none of substantial, specific, and well-established utility, and that credibility of any utility cannot be assessed for said antibody.

Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 5-11 are rejected under 35 U.S.C. 112, first paragraph.

Specifically, since the claimed invention is not supported by either a specific, substantial, or credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

8. In the event that Applicants might be able to overcome the 35 USC 101 rejection above, claims 5-7, 9 and 11 would still be rejected under 35 USC 112 first paragraph because the specification, while being enabling for antibodies that bind to SEQ ID NO: 2, does not reasonably provide enablement for antibodies that bind to polypeptides that are 90% identical to SEQ ID NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re* Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to:

the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention based on the content of the disclosure. See also *Ex parte* Forman, 230 USPQ 546 (BPAI 1986).

The claims are drawn to an antibody, antibody fragment, or single chain antibody that specifically binds to a mammalian polypeptide, which is at least 90% identical to, said amino acid sequence. This means that the claimed antibody is not required to bind residues that are in fact found on SEQ ID NO: 2 and thus the claims read on antibodies that bind to undefined portions of the claimed polypeptide.

In the instant application, the specification teaches that SEQ ID NO: 2 is a form of Zsig9 (p.10, 2nd para.)

One cannot extrapolate the teaching of the specification to the scope of the claims because there is insufficient guidance and direction as to how to make and use antibodies against polypeptides that are at least 90% identical to SEQ ID NO: 2 wherein the antibodies bind to undefined polypeptide sequences because the courts have found that definition of an antibody by its binding affinity to an unknown is not enabling. In particular, the court teaches as follows: "Noelle did not provide sufficient support for the claims to the human CD40CR antibody in his '480 application because Noelle failed to disclose the structural elements of human CD40CR

antibody or antigen in his earlier '799 application. Noelle argues that because antibodies are defined by their binding affinity to antigens, not their physical structure, he sufficiently described human CD40CR antibody by stating that it binds to human CD40CR antigen. Noelle cites En zo Biochem II for this proposition. This argument fails, however, because Noelle did not sufficiently describe the human CD40CR antigen at the time of the filing of the '799 patent application. In fact, Noelle only described the mouse antigen when he claimed the mouse, human, and genus forms of CD40CR antibodies by citing to the ATCC number of the hybridoma secreting the mouse CD40CR antibody. If Noelle had sufficiently described the human form of CD40CR antigen, he could have claimed its antibody by simply stating its binding affinity for the "fully characterized" antigen. Noelle did not describe human CD40CR antigen. Therefore, Noelle attempted to define an unknown by its binding affinity to another unknown. As a result, Noelle's claims to human forms of CD40CR antibody found in his '480 application cannot gain the benefit of the earlier filing date of his '799 patent application. Moreover, Noelle cannot claim the genus form of CD40CR antibody by simply describing mouse CD40CR antigen". *Randolph J. Noelle v Seth Lederman, Leonard Chess and Michael J. Yellin* (CAFC, 02-1187, 1/20/2004).

To reiterate, applicant is claiming antibodies against unknown sequences and since an antibody is defined by its antigen binding capability, claims drawn to unknown antibodies that bind to unknown antigens are not enabled. The specification provides insufficient guidance with regard to these issues and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predictably make or use the broadly claimed antibodies with a reasonable expectation of success.

For the above reasons, it appears that undue experimentation would be required to practice the claimed invention.

9. Claims 5-11 are rejected under 35 USC 112, first paragraph, as lacking an adequate written description in the specification.

Claims 5-11 are drawn to an antibody, antibody fragment, or single chain antibody that specifically binds to a mammalian polypeptide, which is at least 90% identical to, said amino acid sequence. Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Id. At 1567, 43 USPQ2d at 1405. The court also stated that

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics.... i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. " Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here. A disclosure that does not adequately describe a peptide antigen product itself logically cannot adequately describe an antibody to that antigen product.

Thus, the instant specification may provide an adequate written description of the peptide antigens which are at least 90% identical to said amino acid sequence SEQ ID NO: 2, per Lilly by structurally describing a representative number of peptide antigens or by describing "structural features common to the members of the genus, which features constitute a substantial portion of the genus." Alternatively, per Enzo, the specification can show that the claimed invention is complete "by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."

In this case, the specification does not describe peptide antigens in a manner that satisfies either the Lilly or Enzo standards. The specification does not provide the complete structure of any protein which is at least 90% identical to said amino acid sequence SEQ ID NO: 2, nor does the specification provide any partial structure of such peptide, nor any physical or chemical characteristics of the said polypeptide nor any functional characteristics coupled with a known or disclosed correlation between structure and function. Although the specification discloses SEQ ID NO: 2, this does not provide a description of genus of polypeptides to which the claimed antibody is against.

The specification also fails to describe the peptide antigen to which the antibodies are against by the test set out in Lilly. The specification describes only the polypeptide defined by SEQ ID NO: 2. Therefore, it necessarily fails to describe a "representative number" of such species. In addition, the specification also does not describe "structural features common to the members of the genus, which features constitute a substantial portion of the genus."

Thus, the specification does not provide an adequate written description of the claimed polypeptides wherein the polypeptide is at least 90 % identical to SEQ ID NO: 2 to which the claimed antibodies bind that is required to practice the claimed invention. Since the specification fails to adequately describe the antigen to which the claimed antibody binds, it also fails to adequately describe the antibody because an antibody cannot be described by its binding affinity to as unknown antigen.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 5, 6, and 8-11 are rejected under 35 U.S.C. 102(e) as being anticipated by Carter et al. et al. (United States Patent Application, 20040024192, July 1, 1997).

The claims are drawn to an antibody, antibody fragment, or single chain antibody that specifically binds to a mammalian polypeptide said polypeptide being defined by the amino acid sequences of SEQ ID NO: 2 or a polypeptide which is at least 90% identical to said amino acid sequences (Claim 5), wherein the antibody is a monoclonal or polyclonal (claim 6 and 9), a method for producing an antibody which binds to a peptide or polypeptide defined by SEQ ID NO: 2 or to a peptide or polypeptide which is at least 90% is at least 90% identical to said peptide or polypeptide by contacting a cell capable of producing antibodies with said a peptide or polypeptide or a nucleic acid which encodes said peptide or polypeptide and isolating said

antibody (Claim 8), the antibodies of claim 8 wherein said antibody is either a polyclonal or monoclonal antibody (Claim 9), wherein an animal is inoculated with the peptide or polypeptide or nucleic acid under conditions wherein the animal produces antibodies to said peptide; and isolating said antibodies (Claim 10), the method of claim 10 wherein the antibodies are polyclonal or monoclonal antibody (Claim 11).

Carter et al. teach a method of making polyclonal antibodies wherein, in a preferred method, a preparation of the secreted protein is prepared and purified to render it substantially free of natural contaminants. Such a preparation is then introduced into an animal in order to produce polyclonal antisera [0390] wherein it is clear that the protein is brought into contact with cells in the animal that will product the polyclonal antisera. Further, given the above, one of ordinary skill in the art would instantly envision the isolation of the polyclonal antibodies. The reference further teaches antibody fragments [0196], to a polypeptide, SEQ ID NO: 36 (Table on p. 15) that comprises 69 of the amino acids of SEQ ID NO: 2, see attached protein sequence alignment.

Although the reference does not specifically teach antibodies to a polypeptide that is 100% identical to SEQ ID NO: 2, at least a subset of the polyclonal produced by Carter et al. would be expected to cross react and bind to at least an epitope of SEQ ID NO: 2 protein because Cruse et al. (Illustrated Dictionary of Immunology, CRC Press, New York, page 241, 1995) teach that polyclonal antibodies bind to different epitopes on an antigen and represent the natural consequence of an immune response. Thus, Cruse teach that polyclonal antibodies are directed to many epitopes on an antigen and it would be expected that at least a subset of the polyclonal

antibodies of Carter et al, produced against a homologous protein would cross react with and bind to that homologous polypeptide.

The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from that taught by the prior art and to establish patentable differences. See In re Best, 562 F2nd 1252, 195 USPQ 430 (CCPA 1977).

13. No claims are allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter J. Reddig whose telephone number is (571) 272-9031. The examiner can normally be reached on M-F 8:30 a.m.-5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Peter J. Reddig, Ph.D.
Examiner
Art Unit 1642

PJR

SUSAN UNGAR, PH.D
PRIMARY EXAMINER